**NWX-DISEASE CONTROL & PREVENTI (US)**

**Moderator: Dale Babcock**
**July 8, 2015**
**11:00 am CT**

Coordinator: Welcome and thank you for standing by. At this time, all participants are in a listen-only mode. During the question and answer session, you may press star 1 on your touchtone phone if you would like to ask a question.

Today's conference is being recorded. If you have any objections, you may disconnect at this time.

I'd now like to turn the meeting over to Dr. Raymond Strikas. You may begin.

Raymond Strikas: Thank you very much. Welcome to the Current Issues in Immunization of CDC NetConference. I'm Raymond Strikas. I'm a medical officer in the Immunization Services Division of the National Center for Immunization and Respiratory Diseases, or NCIRD, at the CDC. And I'll be the moderator for today's session.

To participate in today's program, you need a telephone connection and a separate internet connection.

The learning objectives for this session are: to describe an emerging immunization issue, be able to list a recent immunization recommendation made by the advisory committee on immunization practices, to locate resources relevant to current immunization practice, and to obtain, assess, and apply patient information to determine the need for immunization.

Today is July 8, 2015. We have one topic for today's NetConference.

Miss Donna Weaver, Nurse Educator in the Communications and Education Branch, Immunization Services Division in NCIRD, CDC will discuss basic principles of vaccination as presented in the CDC textbook Epidemiology and Prevention of Vaccine-Preventable Diseases -- also known as the pink book -- whose 13th edition was published this year.

A question and answer session will follow today's presentation and we will offer another question and answer session on Thursday, July 16 at 10:00 am Eastern Daylight Time for those who could not attend today's session or did not have time to ask a question.

Please make a note of the following information -- if you have technical trouble, please dial star0 on your telephone. If you'd like to ask a question when we get to that segment, please press star1 on the phone.

Continuing Education or CE credit is available only through the CDC ATSDR Training and Continuing Education Online System at http://www2a.cdc.gov/tceonline/. CE credit for this session today expires on August 10, 2015.

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I will now turn the microphone over to Miss Weaver. You may begin.

Donna Weaver: Thank you Dr. Strikas and good afternoon everyone. It's a pleasure to present to you from here in Atlanta.

Now if you're following along in the 13th edition of the pink book, the slides I am using are very similar to the ones in the first chapter. And we also will be posting these slides on the Web site for this webinar series next week.

Also, you should've received an email with external links to videos that will be referred to during this presentation. I will prompt you when it is time for you to click on the link for a video. But be sure that you do not close your link to these slides while viewing the video.

After a video is finished, close that link and immediately return to this link. There are a total of four videos, each with its own individual link and they are each approximately two and a half to three and a half minutes long. And I will prompt you when it's time for the next video.

Please be careful. Due to limited seating, if you close out of this link with the slides, you will not be able to return. So always keep this link open. And then also we will post the videos with the slides next week.

And as I'm sure you know, immunization practice is complicated and getting more complicated every year. New vaccines are introduced and need to be integrated into the schedule. Also, recommendations sometimes change for existing vaccines. And it's easy to get confused.

We found that a discussion of the principles of vaccination and general recommendations for the use of vaccines can help reduce confusion.

So to understand how vaccines work, I'm going to start with some basic information about how the immune system functions.

A healthy immune system is able to recognize and eliminate foreign or non-self-material from the body and ignore everything else that belongs there. In this program, we're going to refer to immunity as protection from infectious diseases.

So this is the immune system's ability to recognize and eliminate infectious agents such as viruses and bacteria and to prevent infection with these agents in the future. This immunity is usually indicated by the presence of an antibody that is specific to a single organism or group of closely related organisms.

There are two ways to acquire immunity -- actively or passively -- and you can have both at the same time. Active immunity is protection that is produced by the person's own immune system and it lasts for a long time -- often a lifetime.

Passive immunity, on the other hand, is protection that is produced by an animal or human and then transferred to another human. The protection is effective but not lasting. It disappears usually within a few weeks or months.

Regardless of the type of immunity, the important thing is the identification of non-self. These foreign substances or antigens can be live viruses or bacteria, or they can be inactivated. The antigen stimulates the immune system to mount a response or defense system that will facilitate the elimination of the antigens, and this generally involves production of antibodies and stimulation of T-cells.

Now, when I was studying the immune system in nursing school, I was taught that antigen is an antibody generator. An antibody is a protein molecule or immunoglobulin produced by B lymphocytes, which are produced in bone marrow. The antibody is specific to a single organism or group of closely related organisms, and it binds to the antigen in sort of a lock and key type mechanism.

When it binds to the antigen, this helps neutralize the antigen so that it cannot multiply, and then other cells -- including phagocytes -- can destroy and remove the antigen from the body.

There are two arms to the immune system. One is humoral immunity, and that's basically what I've been talking about so far. Humoral immunity is essentially the production of antigen-specific antibodies that protect the person who made them, but they can also be transferred to another person to provide temporary immunity.

The other arm of the immune system is cell-mediated immunity, and this involves killer cytotoxic cells, T-lymphocytes, and other components that destroy the antigen. Now, T cells are developed in the thymus gland.

Now, that was a very simplified explanation of what is a remarkable, very complex immune system.

So let's look at the two ways of acquiring immunity a little more closely. As I mentioned earlier, passive immunity involves the transfer of antibodies from an exogenous or outside source that is human or animal to another human. These ready-made antibodies provide temporary protection that disappears or wanes with time -- typically after several weeks or months.

This type of antibody is extremely important to infants who receive antibodies through the placenta before birth. These antibodies cross the placenta to the fetus in the last one to two months of pregnancy. So a full term infant will have the same antibodies as the mother, which are extremely important until the baby can make its own antibodies.

However, these antibodies start to wane -- and some faster than others -- and that's why we have to begin immunizations early in life to protect the baby.

Now, it's time for you to click on the link to the video animation that illustrates the process of passive immunity. And remember, do not close your link to these slides. Close the video link when it ends and return to this link.

Ok I hope everyone's back from the video. And as the video pointed out, there are other sources of passive immunity in addition to maternal antibodies. Blood and many blood products contain antibodies. Washed or reconstituted red blood cells contain a small amount of antibodies compared to intravenous

immune globulin and plasma products, which contain a rather large amount of antibodies.

Now, homologous pooled human antibody -- which is also known as immune globulin or IG -- is just as the name implies. Homologous means the antibodies are derived from the same species and as the name denotes, these are antibodies derived from humans. So these are pooled antibodies from thousands of adult donors here in the United States.

This pooled antibody product contains antibodies to many different antigens. And since there is a large pool of people in the US with antibody to hepatitis A and measles, IG is used primarily for post-exposure prophylaxis for hepatitis A and measles.

It's also used for treatment of certain congenital immunoglobulin deficiencies.

Another type of antibody is homologous human hyperimmune globulin. The source is donated plasma from humans who have a high level of a particular antibody. But these products also contain other antibodies that are present in the plasma. Hyperimmune globulins are used for post-exposure prophylaxis for several diseases -- HBIG for post-exposure to hepatitis B virus and RIG or HRIG for rabies, T-I-G or TIG for tetanus, and VariZIG for varicella.

And do you know what V-I-G is used for? Well, it's vaccinia immune globulin that can be used to treat severe adverse reactions to smallpox vaccine.

Heterologous hyperimmune serum, also known as antitoxin, is produced by animals -- usually horses. So it is an equine antitoxin. The serum contains

antibodies to only one antigen. In the US, antitoxin is available for treatment of botulism and diphtheria.

Now, one downside associated with antitoxin is serum sickness. The body has an immune reaction to the foreign protein that is similar to an allergic reaction. Tetanus equine antitoxin was used primarily before World War Two and there could be some older persons who report being allergic to tetanus vaccine when what they actually experienced was serum sickness to the equine antitoxin.

Now, there is no horse protein in tetanus immune globulin or any of the tetanus-containing vaccines.

Antibodies from human sources are polyclonal, meaning they contain many different kinds of antibodies -- some in more quantities than others. But scientists came up with a way to isolate and indefinitely grow single B cells when then led to the development of specific or monoclonal antibodies.

A monoclonal antibody contains antibody to only one antigen or a closely related group of antigens. Monoclonal antibodies are used in the diagnosis or treatment of certain cancers, also in prevention of transplant rejection, and the treatment of certain autoimmune diseases and infectious diseases.

One monoclonal antibody product you may be familiar with is Palivizumab or Synagis. This is an antibody product available for the prevention of respiratory syncytial virus, or RSV infection, in infants.

Now, there's been a lot of confusion about this product. Although it is used to prevent severe RSV disease, it contains only RSV antibody. It is not a vaccine. But the good news is that since it is a monoclonal antibody, it will

not interfere with the immune response to vaccines -- especially live vaccines like MMR and varicella.

So now I'm going to move onto the other way of acquiring immunity -- active immunity. Active immunity is really the best type of immunity. Sometimes people refer to this as natural immunity.

Now, it's produced by the person's own immune system and it's usually long lasting, often for a lifetime.

So now it's time to click on the link to a short video animation that illustrates the process of active immunity. Again, remember do not close this link to the slides. Ok, welcome back.

So there are two ways to acquire active immunity. One is infection with the disease-causing form of the organism. Examples would be the protection or immunity that develops after infection with measles or chicken pox. Second infections can occur, but they are not common if the person has a healthy immune system. And typical second infections -- if they do occur -- are usually asymptomatic.

After the initial infection, there are memory B cells in the blood and bone marrow that remain there for many years. So if there's a reexposure to the infectious agent, these memory cells go into action to produce antibody and eliminate the antigen.

The good news is that active immunity can also be acquired with vaccines without getting the actual disease, the discomfort that associates it, and potential complications.

Vaccination is a way of stimulating the immune system when exposed to a live, weakened form of the organism that does not cause disease in someone with a normal immune system or when exposed to an inactivated form of the pathogen or disease-causing agent. The vaccine delivers this weakened or inactivated antigen that induces an immune response that is similar to the response to natural infection.

Many vaccines also produce memory B cells. This immunologic memory allows for what is referred to as an anamnestic response. In other words, when there is a reexposure to the antigen, the memory cells begin to produce antibodies that go into action against the antigen.

Now, there are many factors that influence a person's immune response to a vaccine. One is the presence of maternal antibodies, which have more effect on live vaccines because they cannot tell the difference between the disease-causing antigen and the live, weakened antigen. This is why only oral live vaccine is administered during the first year of life, because the immune response is not affected by circulating maternal antibodies.

Other factors that affect the immune response to a vaccine are the nature and amount or dose of antigen in the vaccine, the route of administration, and whether an adjuvant is present to improve the vaccine's ability to provoke an immune response and also whether the vaccine has been stored and handled properly.

There are also factors about the person receiving the vaccine that influence the immune response to the vaccine. And these include age, nutritional status, genetics, and any coexisting disease.

There are two basic classifications of vaccines. The characteristics are different and determine how the vaccines are used.

A live attenuated vaccine contains a weakened form of the wild disease-causing virus or bacterium. An inactivated vaccine contains inactivated or dead virus or bacterium or a fraction of the organism.

Now, in order to simplify some of the principles of vaccination, we've developed a few general rules. So if you're following along in the pink book, you'll find these general rules in boxes in the text in the chapters on principles of vaccination and general recommendations.

And here's the first general rule -- the more similar a vaccine is to the natural disease, the better the immune response to the vaccine. Now, this makes sense since disease-induced immunity is generally solid and long lasting. And the closer we can approximate that with vaccines, the better the protection from the vaccine.

So from this rule, you would expect that live vaccines would have some advantages, since infectious diseases are caused by live organisms.

So now it's time to click on the third video that illustrates how live vaccines work. Remember, don't close out your link to these slides.

Ok, the wild virus or bacterium is weakened by repeated passage in culture media. It took almost ten years to transform the wild measles virus that was obtained from a child with measles disease in 1954 before it could be used to make vaccine.

An important characteristic of a live, attenuated vaccine is that the organism can replicate or multiply to provoke the immune response -- just as the wild organism would do. And since the response is so similar to the immune response produced by natural infection, a live attenuated vaccine will generally produce an immune response in most recipients with one dose.

Now, there are exceptions. Live oral vaccines are not delivered by injection, but rather into the digestive system or the gut. So they require additional doses, as was the case with oral polio vaccine and now with the rotavirus vaccines and also one of the typhoid vaccines.

Also, there's a small percentage of vaccine recipients that do not respond to the first dose. And most of these persons do respond to a second dose.

This graph illustrates an individual's response to a dose of live vaccine. The Y or vertical axis represents the antibody level, and the pink line represents the antibody level that is protective. The X or horizontal axis represents the number of doses administered. So you can see that after one dose of the vaccine, a positive response to the vaccine is well above the protective pink line.

Administering subsequent doses really doesn't improves the antibody level that much, and if you look out further through time, there's very little waning of the immune response.

This graph, on the other hand, looks at population response to a live vaccine. The Y or vertical axis represents the percent of the population or community that is immune. And the X or horizontal axis represents the number of doses administered.

As with the individual response, you see that the population or community immune level is quite high after just one dose and rises gradually as the small percentage of those who did not respond to the first dose receive a second dose. And a third dose shows really little difference.

Now, what that second illustration was addressing is what we refer to as herd or community immunity. This slide represents three communities. In these communities, blue figures represent people who are not immunized but they're still healthy. Yellow figures represent people who are immunized and healthy. And the red figures represent those unfortunate people who are not immunized and they're sick and contagious.

The first community is shown on the left. Initially does not have very many sick people. But there are lots of susceptible people -- most of whom become sick and contagious, as you see on the right side.

Now, in the left illustration of the second community, there still are not very many sick people. But there are also some healthy immunized people. But there aren't very many, so on the right you can see that there is still a lot of disease spreading.

And last but certainly not least is the illustration of a community with a high immunization coverage rate. Although there is still the same initial number of sick people on the left, there is very little disease on the right because the spread of the disease is contained.

Now, this is a very simplified illustration of herd immunity. The herd immunity threshold -- or proportion of the population that must be immune to stop disease transmission -- varies by disease. Some of the factors that influence this threshold are how contagious the organism is, how it's

transmitted, and how people interact with each other and whether the disease is endemic or it comes in epidemic waves.

There are some things that we need to be aware of with live vaccines. Even though they are weakened and generally do not cause disease or anything more than a mild adverse reaction in someone with a healthy immune system, they can cause severe or fatal reactions in people who are immunodeficient -- whether due to disease, medication, or treatment such as radiation. Because a person who is immunodeficient may not be able to mount an effective immune response and a level of antibodies that will stop the replication of the vaccine virus.

It is also theoretically possible for the live attenuated virus to revert to the disease-causing form. Now, this has only been known to occur with oral polio vaccine.

It's also possible for circulating antibody to interfere with the immune response to a vaccine. As I mentioned earlier -- and was pointed out in the video -- circulating antibodies, whether maternal antibodies or from other products, cannot tell the difference between the wild organism and the attenuated organism.

So, conducting thorough screening before administering a dose of vaccine is the most important strategy to preventing not only allergic reactions but a serious or fatal reaction in an immunodeficient person, or in preventing vaccine failure because of the presence of circulating antibodies that interfere with the immune response.

And another important strategy is to be sure -- like I said earlier -- that vaccine storage and handling protocols are followed to prevent administering a vaccine that's not effective.

Live vaccines especially are fragile and must be stored and handled according to the vaccine manufacturer's recommendations.

There are currently several live attenuated viral vaccines available -- measles, mumps, rubella, varicella, and zoster vaccine, yellow fever, rotavirus, and the intranasal influenza vaccine. Also vaccinia and oral polio vaccine, which is available in other countries but is not used in the US.

The only live attenuated bacterial vaccine used in the US for vaccination is oral typhoid vaccine. The BCG tuberculosis vaccine is not routinely used to protect against tuberculosis in the US. It's actually used to treat bladder cancer.

So now, let's take a look at inactivated vaccines. The virus or bacterium is inactivated with heat and/or chemicals like formalin. There are two main groups of inactivated vaccines -- those that contain inactivated whole virus or whole bacterium, and a large second group which are referred to as fractional vaccines.

Fractional vaccines contain only immunogenic pieces of the organism. And among the fractional vaccines, most are protein-based such as subunit vaccines and toxoids. Some fractional vaccines are polysaccharide based and may be either pure polysaccharide or conjugated polysaccharide.

Ok it's now time to click on the link to our last video about inactivated vaccines. And then I'll see you back on this link for the remainder of the presentation.

Now, a key message in this video is that unlike live vaccines, inactivated vaccines cannot replicate. So there's no way inactivated vaccines can result in infection from the antigen and the vaccine, even in immunodeficient persons. The antigens are dead.

And inactivated vaccines are less affected by circulating antibodies than live vaccines. So maternal antibodies have little or no effect on the immune response to the vaccine. And when necessary an inactivated vaccine can be administered at the same time as an immune globulin.

An example is the administration of hepatitis B immune globulin and hepatitis B vaccine at the same time, in separate anatomic sites to an infant born to a mother who is hepatitis B surface antigen positive. The ready-made antibodies in the immune globulin provide protection through passive immunity until the baby can mount an active immune response to hepatitis B vaccination.

The amount of antigen from a dose of inactivated vaccine is fixed. Since there is no replication, multiple doses are required before a protective antibody level is reached. And the immune response is primarily humoral. There is little if any cell mediated immunity.

The antibody titer, or level of antibody, will decline with time and periodic booster doses may be required.

Unlike the graph shown earlier for live vaccines, the antibody level is not usually at a protective level after a single dose with inactivated vaccine. The

first dose primes the immune system and then it takes two to three more doses before a protective antibody level is reached. Then, as the last column shows, the antibody level begins to wane. An example would be the DTaP series. That is why it is so important that parents understand the need to continue the vaccination series as recommended and for pregnant women to receive their Tdap dose and pass on those maternal antibodies to their baby. One or two doses of DTaP vaccine does not protect the young infant against pertussis, and they're usually two months old before they start the series.

The population response to vaccination with an inactivated vaccine also looks very different than it did for a live vaccine. It takes several doses for each person before a high percentage of the population is immune and there's a barrier of protection within the community.

Inactivated whole virus vaccines available in the US include inactivated polio, hepatitis A and rabies. Inactivated whole bacterial vaccines include the whole cell pertussis vaccine, killed typhoid, cholera, and plague vaccines.

Now, these inactivated whole bacterial vaccines and the whole influenza viral vaccine are really now only of historic interest, since none of them are used in this country.

Some vaccines can be made using only certain proteins from the organism that will produce the immune response. Subunit vaccines include hepatitis B, influenza, acellular pertussis, human papillomavirus, and anthrax.

Now, diphtheria and tetanus vaccines are made from toxins produced by the organisms. The toxins are inactivated and then referred to as toxoids. Polysaccharides are complex sugars that make up the outer coat of certain bacteria, most notably the meningococcal, pneumococcal, and haemophilus

families. The polysaccharide coat is important in the development of disease and immunity. So one would think that making a vaccine using this outer coat would be fairly straightforward -- just purify the polysaccharide and put it in a vial. And basically that's how pure polysaccharide vaccines are made.

But, there's a catch -- the immune response to a pure polysaccharide vaccine is typically T-cell independent. In other words, these vaccines stimulate B cells without the assistance of T-helper cells. But polysaccharide vaccines are not very immunogenic in children younger than two years of age. Most likely because their immune systems are still immature.

And repeat doses usually do not cause a booster response. Also, IgM antibody is the predominant antibody produced, and there's little switching over to IgG antibody. IgM antibody has less functional activity than IgG.

But the good news is that polysaccharide vaccines can produce a better immune response when chemically combined with a protein. And this is referred to as conjugation, which changes the immune response from T-cell independent to T-cell dependent. This increases the immune response in infants and the antibody booster response to multiple doses of vaccine.

There are both pure polysaccharide and conjugate pneumococcal and meningococcal vaccines. All Hib-containing vaccines are conjugate. And the inactivated injectable typhoid vaccine is a pure polysaccharide vaccine.

There are some vaccines that are developed through genetic engineering technology, where a gene segment of the antigen is inserted into a different microbe or microorganism and then cultured on a large scale to make the vaccine. For example, hepatitis B surface antigen and then grown in yeast cells to make the vaccine.

Vaccines that contain recombinant components are -- as the one I just mentioned -- hepatitis B, also human papillomavirus, the RIV3 influenza vaccine, and then the meningococcal B vaccines do contain recombinant proteins.

Reassortant vaccines are vaccines made by mixing genetic material from more than one source. The RV5 rotavirus vaccine contains genetic material from both human and bovine or cow strains. And each of the four influenza viruses in live attenuated influenza vaccine contain gene segments from different viruses.

Ok I want to turn briefly now to the recommended immunization schedules. This is the recommended childhood and adolescent schedule for 2015. The recommended vaccines are in the far left column and the ages at which various doses are recommended are across the top.

You will notice that with the exception of the oral rotavirus vaccine, only inactivated vaccines are recommended in the first year of life because of the presence of maternal antibodies. The antibodies wane within a few months, and generally by 12 months of age they will no longer interfere with the immune response to live attenuated vaccines like MMR and varicella.

You can also see that the inactivated vaccines require between three and five doses for a complete series, whereas only two doses are recommended for MMR and varicella. The second doses of these live vaccines like I said are recommended to catch the small percentage of children who did not respond to the first dose.

Now, the yellow bars indicate the age range in which a particular dose is recommended. The green bars indicate the range of recommended ages for catch-up immunization. And the purple bars indicate the range of recommended ages for high-risk groups for certain vaccines.

There are also two catch-up schedules shown here on this slide. The top schedule is for children four months through six years of age who are behind schedule for one or more vaccine series. And the schedule below the heavy black line is for children seven years through 18 years of age who are behind.

Now, these schedules should be used until the child is caught up and then return to the routine schedule.

The timing of doses is based on the minimum ages and minimum intervals, which will be discussed in more detail during the next two sessions on general recommendations.

There are two adult schedules for persons 19 years of age and older. The same color coding convention used for the childhood/adolescent schedule is used here for recommended age ranges and for high-risk groups. This first adult schedule is based on recommended ages for particular vaccines if the person has no other evidence of immunity or for recurring doses, such as annual influenza vaccination and TD booster doses every ten years.

The second immunization schedule for adults is based on risk factors, such as medical, lifestyle, or occupational risks for healthcare personnel. The addition of the red bars indicates a contraindication for the live vaccines varicella, zoster, and MMR, when a woman is pregnant or in the case of immunodeficiency.

Ok so now before I take your questions, I'd like to ask you a question. I want you to tell me if the following statement, if you think it's true or false. Because pure polysaccharide vaccines like the pneumococcal polysaccharide vaccine, PPSV23, and the meningococcal polysaccharide vaccine are T-independent, they provide good booster responses with subsequent doses. So make your selection and just click on that little circle either next to true or false. And we'll give you a few seconds and then we'll see how everybody's doing.

Ok let's see how everybody did. You can see that well, it's not exactly 50-50 but its close. More persons selected false, which actually is the correct answer. You know, we think of being independent as being a good thing, right? But in the case of polysaccharide vaccines, they do not produce a good booster response. However, conjugating them to a protein improves the booster response as well as the overall immune response in children younger than two years of age by making them T-dependent so that you get the help from the T-cells.

All right so with that, I'm going to turn things back over to Dr. Strikas so we can take some questions from you.

Raymond Strikas: Thank you very much, Miss Weaver. I'd like to now invite our listeners to call in and ask questions. To do that, please dial star 1 on your telephone. Please restrict your questions to the contents discussed during today's presentation. Please also tell us your first and last name and where you are from. And now I'll temporarily turn the microphone over to our operator.

Coordinator: Thank you. And once again, if you'd like to ask a question, press star 1 and record your first and last name clearly when prompted. One moment please as we wait for our first question.

Raymond Strikas: While we're waiting for that first question, I'd like to provide some additional information.

First, a recast as well as the slide set will be available on cdc.gov/vaccines/ed/ciinc, as you see on the slide, during the week of July 13th -- it says July 15th on your slide, but during the week of July 13th, 2015 -- that is, next week.

For CE or continuing education credit, please go to the Web site listed above -- www2a.cdc.gov/tceonline. The course number for this Net Conference is EC2064. The verification code is Epi-POV and the CE credit expires on August 10th, 2015 for today's session.

Let's see if we've got a question in the queue.

Coordinator: We have several questions in queue. And the first one comes from (Jane). (Jane), you have an open line.

(Jane): Good morning and thank you for this presentation. Often when we give vaccine for immunity for influenza for the flu season, I have people always want to counter that they, even though they received the non-live vaccine, that they get the flu. And I know that all the documentation speaks to there being the two-week period before they can have immunity to the flu vaccine and that they, you know, probably had it before they got the vaccine.

Is there any other information that you can provide that can help counter that? Because I have people that would die on the cross to say that they get sick from the vaccine.

Donna Weaver: Well, hi (Jane). That's an excellent question, and one that we get a lot. Like I said, inactivated vaccines, the organisms are dead. It is not possible for them to cause the influenza disease.

Now, there can be some side effects to the vaccine. I mean, they may have, you know, in addition to a sore arm, they could have a little bit of aching and not feeling so great for a couple of days as the immune response is mounted. And as you said, it does take a couple of weeks before, you know, they have a full protective immune response -- around two weeks, we say.

But it is possible that they could have been already incubating -- infected before they got the vaccine. So yes, they actually could have the flu.

The other thing is, you know, we do the best possible that we can to select the viruses that are going to be circulating in a season to put into the vaccine. But as you know last year, we didn't have as good a match as we had hoped for because one of the viruses drifted after they started to manufacture the vaccine and it's not easy to just switch horses in the middle of the stream.

So it is possible that they could have been infected with a strain that wasn't in the vaccine, or a strain that drifted. So it's possible, but it's not possible to get flu from the flu vaccine, the inactivated vaccine. And really, not even from the live attenuated vaccine. They may have some, you know, little bit of runny nose and feel a little bit like I said aching or cough, but you can't get the flu from the flu vaccine. I hope that helps.

(Jane): Thank you.

Coordinator: Our next question comes from (Barbara Ottis).

(Barbara Odis): Hi. Thank you for taking my question. So with the measles situation recently, and there was an outbreak in a daycare center near Chicago and all those kids were under 12 months of age, I worry about why we're seeing disease in those kids that may still have maternal antibody.

I'm wondering whether there's ever been or currently any discussion around lowering the age for that first dose of MMR.

The other thing I worry about is those teenagers who may be having babies right now who never got even one dose of MMR and aren't giving their infant any maternal antibody protection.

Donna Weaver: Well, as far as discussion about decreasing the age, I know that in, you know, that age over the years has kind of moved back and forth. And I know that that's something they, you know, continue to monitor because the babies that are born to moms who were vaccinated rather than actually had measles do have less maternal antibody.

But at this point, I've not heard of any discussion. I ask Dr. Strikas if he wants to add to that.

Raymond Strikas: Yes, I would add that it is the prerogative of local health departments that in the setting of an outbreak, they could vaccinate children down to six months of age if they felt that was an important outbreak control measure. I don't know what the situation in Chicago was, but it is an option one can consider. And CDC just made the point that one can consider that.

As Miss Weaver said, maternal antibody's a moving target and it's a continuum and it diminishes -- pretty much gone by 12 months of age. But because we want to be sure the children are protected when they receive their

first dose of MMR if at all possible the current recommendation is to vaccinate between 12 and 15 months of age for that first dose.

If you vaccinate any younger, the concern is -- and it varies from population to population -- maternal antibody may interfere with any of the three components of the MMR vaccine. And so absent travel or absent an outbreak situation, we're not recommending routine vaccination below 12 months of age. And I'm not aware that our Advisory Committee on Immunization Practices will be considering that issue in the near future.

Donna Weaver: And something else to point out is that if we do administer a vaccine to a child between six and eleven months of age, that dose will not count as one of their two what we call valid doses that they need on or after the first birthday. So the valid doses have to be given on or after the first birthday and must be at least four weeks apart. Of course, generally that second dose is given when they're getting ready to go to school at four to six years of age.

Now, regarding teens having babies that did not get vaccinated, that's not good for mom or baby. I mean, I think again these are things that we need to try to educate people about. And there's been I think a lot more going on in terms of education with the measles outbreaks that have occurred. Certainly, we don't want to have to have outbreaks to educate people, but it has put it back on the radar. People just, you know, out of sight, out of mind. And when you weren't seeing measles very much, people felt like well why bother getting vaccinated?

And I think that the media has also picked up on this and really been promoting people being vaccinated. So...

(Barbara Ottis): Can I ask...

Donna Weaver: ...you know - go ahead.

(Cross talk))

(Barbara Ottis): ...one other question? I was just thinking about our newly pregnant women and how they're checked for rubella status, but doesn't seem like we're paying that much attention to their MMR status, to the measles part. And I'm not sure if ACOG has changed that, but it seems like we're just focusing on rubella.

Donna Weaver: Well, you know, yes I think the big thing during pregnancy is because, you know, especially if that woman were to become infected with rubella in the first trimester that it really can have serious or deadly consequences to the fetus.

(Barbara Ottis): Indeed. But we only have two cases of rubella right now in the whole 2015.

Donna Weaver: Yes, fortunately.

(Barbara Ottis): It just seems like ACOG needs to give us a stronger recommendation about assessing measles status. Just a thought.

Raymond Strikas: Thank you very much. Can we have the next question please?

Coordinator: Sure. Our next question comes from (Patty Sheldon) from Ventura County.

(Patty Sheldon): Hi. I appreciate the conference. This is really interesting. I had a question in regards to the recommendation for the live zoster vaccine and the contraindication if the patient is immunocompromised.

You know, I understand if you have a severely immunocompromised or an HIV patient or whatever, but I've had people ask me specifically. They're relatively healthy but they've got asthma so they're on inhaled steroids constantly, you know, daily. And then periodically once, twice a year maybe they have a short course of oral steroids. And now they're concerned. Does that make them fall into that category where they're considered enough immunocompromised that they shouldn't take a live like the zoster vaccine?

Donna Weaver: Actually, there's good guidance on that in the ACIP General Recommendations about immunodeficiency and especially with corticosteroids. We typically don't think of inhaled steroids as being a contraindication, and even a short course of steroids typically, you know, less than two weeks, would not cause a problem. Maybe not vaccinate while they're...

(Patty Sheldon): Right.

Donna Weaver: ...on the course. But as far as inhaled steroids, that typically is not a problem. And again, it's a clinical decision, you know, for...

(Patty Sheldon): Right.

Donna Weaver: ...that person's provider if they feel that they really are significantly immunodeficient or...

(Patty Sheldon): Yes.

Donna Weaver: ...immunocompromised.

(Patty Sheldon): And that's I think kind of what the doctors are finally deciding. I refer them back to their provider for that. And that was the question. They were a little nervous. Some of them had had a course of shingles in the past and didn't want to get it again, but then they were weighing their options. What is the chance that by getting this vaccine, I might get it because I'm, you know, taking - and I understand the inhaled steroids should be a very low risk. But anyway, thank you very much.

Donna Weaver: Well, and take -- like I said -- take a look at that. There's quite a significant discussion about that in the ACIP General Recommendations.

(Patty Sheldon): Ok.

Donna Weaver: And them some more guidance in the zoster recommendations. These are online. And if you have trouble finding this stuff, just email us at NIPInfo and we'll be happy to help you find it.

(Patty Sheldon): Ok.

Donna Weaver: But you know, I think that as they gain more information about this, there will be more guidance about which medications or the amount that you need to be concerned about with giving the zoster vaccine.

(Patty Sheldon): Perfect. Thanks so much.

Donna Weaver: Yes.

Raymond Strikas: Thank you. Next question please.

Coordinator: Next question comes from (Alaska).

(Alaska): Hi. We - I just wanted to see if you can talk more about the T-cell memory and the different types of vaccines and if T-cells have any memory.

Donna Weaver: Well I think the immune memory primarily is stimulated - it comes from the B cells. And I'm not sure I understood the remainder of your question.

(Alaska): So...

Donna Weaver: You mean the difference between like humoral immunity and cell mediated immunity?

(Alaska): Right or live vaccines versus inactivated or, right.

Donna Weaver: Well, both can certainly stimulate the immune system. You know, obviously the live vaccine is closer to what actually happens with natural infection. But both can produce - it really depends on the specific organism that we're talking about that whether there's immune memory.

And then the other thing that plays into that is not only whether the vaccine induces immune memory, but is there time to mount an immune response if the titer has waned. For example, like with hepatitis B, there's a long incubation period so there's really time for -- even though the antibody titer may have waned -- if the person has responded there's time to mount that immune response and that occurs, you know, with an inactivated vaccine.

Whereas with meningococcal disease, even though the vaccine may mount an immune response and have immune memory, that incubation is so, so short with that there really isn't time for that anamnestic response to occur and help.

Dr. Strikas, you want to chime in on this?

Raymond Strikas: Yes, I think you've covered it, Miss Weaver and I think the issue is it does vary by vaccine. You know, we've got data for vaccines such as hepatitis B and HPV that are inactivated vaccines, but the duration of protection seems to be as long out as we follow those vaccines. And for hepatitis B, it's over 22 years. For HPV it's beyond ten years. And it's just got to do with the composition of the vaccine and whether it stimulates T-cells. And there's a host of different T-cells and the T-cell effectors that are in play here. So it varies by vaccine type.

I will commend those who wish to read more about it. And we have limited time to discuss it beyond the pink book, that the textbook Vaccines edited by Plotkin and colleagues. The chapter two is on vaccine immunology and there's a great deal more information there that you may find of benefit.

Can we go to the next question please?

Coordinator: Yes. Our next question comes from (Lisa Dilette).

(Lisa Dilette): Hi this is (Lisa). My question is in regards to the hepatitis B vaccine, because this question always comes up and sometimes people get, you know, their regular series of hepatitis B, don't have a problem. But then later on when they get checked to see if they have had the series -- because they don't remember and their mom didn't tell them -- it doesn't show that they've had immunity.

My understanding is that if you expose them to another vaccine that that would show that they've - it's like a way of boosting it or showing that they do have immunity. Can you speak to that at all?

Donna Weaver: Yes, and this is a common question that we get. With the hepatitis B vaccine, like I mentioned in one of the previous questions, you know, number one -- it only counts if they have a documented series. I kind of use the phrase that I learned in nursing school, "If it ain't written, it wasn't done." So if you don't have documentation of the series, then, you know, vaccination with the series would be recommended.

Now, in terms of if you have documentation that they've received the vaccine and then let's say they got it, you know, as a routine adolescent vaccine or childhood, and now they're getting ready to go to medical school or nursing school or something and they test them. And the antibody titer is low. It's not high enough to show that it's positive. And so you don't know then if you've got documentation. Well, is this telling me that they never responded to the vaccine, that they were a non-responder, or is it telling me that the antibody has just waned?

So what you can do is give a dose of vaccine and what's in there is hepatitis B surface antigen. That's what's in the vaccine. So it will then, if they were a responder, it will stimulate that anamnestic response. It's really a challenge dose, you could say. And then the antibody titer will go up. And then if you test them -- typically a month, four to six weeks -- after that dose, then if they were originally a responder, then you'll get a positive response of 10 mIU/mL or greater and you just document that along with the fact that, you know, make sure that their vaccine doses were documented.

And that's it. You send them on their way with a copy of their immunizations and a copy of their lab report as well as keeping it in their medical record. And they should keep that with them. And then there's no booster doses or anything recommended.

But now, say after that dose, they still don't respond. Then the recommendation is to give them two more doses to complete a second series of hepatitis B vaccine using the normal intervals between doses. And then after that last dose, the third dose of the second series -- so now they've have a total of six documented doses -- then you check their titer again -- typically four weeks after that last dose-- and if it's positive, again, document it, make sure that the lab is documented, the serology, and then also that they have a copy, and that's it. They're good to go.

If it turns out that they're still negative, then if you haven't already done so, check their hepatitis B surface antigen status, because if they're positive, it could mean that they were actually infected with hep B and that's why they didn't respond to the vaccines.

But it also then could mean that they're a hypo-responder or a non-responder, and should they ever have an exposure, they would have to, you know, follow the protocol for hepatitis B immune globulin to protect them.

And there was guidance that came out from CDC. I can't remember if it was a couple of years ago. I'd be happy to direct you to that if you want to send in just a reminder to me in NIPInfo and we can direct you to where that document is on our Web site that goes through all of this. And there's an algorithm for this as well as the latest table on what to do for post-exposure prophylaxis.

And also the Immunization Action Coalition -- which is one of my favorite Web sites -- www.immunize.org has a job aide or a handout with this algorithm on it also.

So I hope that helps.

(Lisa Dilette): Thank you.

Raymond Strikas: Yes this is Dr. Strikas, and the reference Miss Weaver was referring to is in the Recommendations and Reports, the Morbidity and Mortality Weekly Report in December of 2013. If you go to cdc.gov/mmwr and click on publications, recommendations, and reports and then go to 2013, you'll see it as the final publication. And it's on hepatitis B post-exposure prophylaxis.

Can we have the next question please?

Coordinator: Our next question comes from (Cheryl Sorrino).

(Cheryl Sorrino): Yes I'm asking a question about HPV9 and that anamnestic response. What I'm understanding is that pharmaceutical companies are saying that it can go - that the protection goes out eight to nine years and maybe beyond ten years.

But I'm wondering do they also believe that there's an anamnestic response to HPV9 that should they actually have been confronted with the antigen, that they would be protected long after ten years? Because I think some of the people might be thinking if you're giving a 12 year old HPV and its only lasting ten years -- just when they're at the prime sexually active age -- they may not be getting the protection.

Is there any information about that?

Donna Weaver: Dr. Strikas, I don't know that there's data that far out with any of the HPV vaccines.

Raymond Strikas: Yes, the problem is, or the challenge is we only have data out to ten years. And my understanding of the data is they are robust out to that period of time, but given the vaccines were first distributed licensed in 2005-6 and the studies were done of course before that, published data that we're aware of only go out to about the time you mentioned.

There is no reason to think protection won't last longer because of the durability, the apparent durability of the protection and antibody studies for what we have available. But we only have what we have. And so there is no anticipation at present about talking about booster doses of either HPV or for that matter hepatitis B vaccine, because both seem to be very different vaccines or both seem to have very durable antibody after a primary series for the period of time studied.

(Cheryl Sorrino): Thank you.

Raymond Strikas: Can we get - one more question we'll answer.

Coordinator: Question comes from (Andy Huego).

(Andy Huego): Hi. I just wondered, you said that live vaccines don't cause disease. And I was just wondering what's the results from the replication of attenuated bacteria or virus that you talked about happened.

Donna Weaver: Well, a live vaccine is an attenuated vaccine. It has been weakened so that there's enough there that will cause - that the replication will stimulate the

immune response until there's enough antibody there to stop replication and so the disease does not occur.

Now with inactivated vaccines, there's no replication and it's not alive so it can't cause disease.

The problem comes in most often with the live attenuated vaccine if the person is immunocompromised, especially if they're severely immunocompromised, then they may not be able to stop that replication even of the attenuated or weakened live virus or bacterial product that's in the vaccine. And so, they can't - it overwhelms their system and then they can become infected. It can be very serious or even deadly to them.

That's why it's so important to screen for persons who are immunocompromised when it comes to live vaccines.

Raymond Strikas: Ok.

(Andy Huego): Just a follow-up I guess. It can infect them just because there's more cells and there's more of a chance for it to revert to a non-attenuated form or - I don't understand.

Donna Weaver: Well, it - no it's just that there's so much of it. And if they don't develop antibody, if you get enough even of the weakened organism into the body and you can't develop enough antibody, you know, to protect against it, even the weakened form can cause disease. It's not necessarily that it reverts to the wild form.

(Andy Huego): Ok.

Donna Weaver: Dr. Strikas?

Raymond Strikas: No, I agree and, you know, this has been rarely documented with measles containing vaccines with infections and severely ill HIV infected persons. There's been at least one fatality related to vaccine-derived measles virus. And of course, with oral polio viruses, we saw regularly -- though it was rare -- the vaccine viruses caused paralytic disease in a small number of people annually, which is why we are no longer using an activated polio vaccine and the world is moving away from oral polio vaccines as we get closer to polio eradication.

I think that's our last question. So let me wrap up, because we're running out of time. I want to thank everyone for participating today. Thank you, Miss Weaver for the presentation. And let's move to some closing information and look at some housekeeping items.

For continuing education credits, please go to the Web site I've mentioned before -- www2a.cdc.gov/tceonline. The course number for today's program is EC2064 and I was told I read the verification code too quickly, so here it is again -- Epi-POV. I'll repeat that -- Epi-POV, the verification code for today's program. And the CE credit will expire on August 10, 2015 for today's program.

Once you become familiar with CDC's online CE system, you'll find it easy to use and a great way to keep track of your CE credits earned from CDC training programs.

If you have any difficulty with that program or you're new to the system, you can get assistance by phoning 1(800)41TRAIN, T-R-A-I-N or 418-7246 with

availability of staff to answer your questions between 8:00am to 4:00pm Eastern time.

To get help by way of email, you can contact CE@cdc.gov.

We've received many good questions today, and if you were unable to ask your question today or you have other questions related to this NetConference, you have several options -- one of which is you can contact us by email at our question and answer service on immunization issues at NIPInfo@cdc.gov. That's NIPInfo@cdc.gov.

You can also join a repeat Q&A session on today's topic, Principles of Vaccination eight days from now on July 16th Thursday at 10:00 am Eastern Daylight Time. Registration information for that Q&A session will be at the Web site where you saw information about registering for today's NetConferences.

Today's presentation slides, audio material, and transcript will be available at that CDC NetConference Website, again where you registered for today's NetConference.

Another way you can ask a question is contact the CDC Info Program, which is s general CDC information Web site or phone number. You may call 1(800)CDC-INFO. This phone line is there from 8:00 am to 8:00 pm Eastern Time Monday through Friday.

Another way to contact the CDC Info Program is go to the CDC home page -- www.cdc.gov and click on the CDC Info link at the bottom of the page. This is a general question and answer service that handles many questions,

including immunization-related questions as well as other public health-related questions.

I really want to thank everyone for joining us today, with special thanks to our subject matter expert Miss Donna Weaver. Please join us next week for a discussion about general recommendations on immunization and our next NetConference in this series. And thank you very much from Atlanta and have a great day. Good day.

Coordinator: This concludes today's conference. Thank you for joining us. Participants may now disconnect.

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